Claims 7 and 14 stand rejected under 35 U.S.C. §103(a) as allegedly obvious in view of U.S. Patent 6,127,120.

The foregoing rejections constitute all of the grounds set forth in the August 4, 2003 Official Action for refusing the present application.

Applicants note that the Examiner is correct in presuming (at the top of page 6 of the August 4, 2003 Office Action) that the subject matter of the various claims was commonly owned at the time the inventions covered thereby were made.

CLAIMS 1, 5, 6, 8-13, 15-19, AND 37 ARE NOT ANTICIPATED BY U.S. PATENT 6,127,120

The Examiner has rejected claims 1, 5, 6, 8-13, 15-19, and 37 under 35 U.S.C. §102(e) as allegedly lacking novelty over the disclosure in U.S. Patent 6,127,120.

In support of the 35 U.S.C. §102(e) rejection, the Examiner provides, at pages 3-5 of the Official Action, specific citations to U.S. Patent 6,127,120 which allegedly teach the claimed invention. Specifically, the Examiner contends that the combination of the Abstract; claims 1, 2, 8, and 36; column 13, lines 37-43 and 57-65; column 38, lines 22-25; and Examples 1-9 of U.S. Patent 6,127,120 teach the method as claimed in claim 1(a) of the instant application.

It has been recognized that a rejection under 35 U.S.C. §102(e) is warranted only when the cited reference identically discloses the subject matter of the invention as claimed. In re Bond, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990).

Applicants respectfully submit that nowhere in U.S. Patent 6,127,120 is there a teaching or suggestion of a method for detecting the presence of a target nucleic acid sequence employing surface enhancement by the aggregation of a metal (colloid) surface that is caused by and dependent on the presence of a target sequence. In other words, U.S. Patent 6,127,120 fails to teach a detection method which is carried

out by the combining of a sample with metal (colloid) in non-aggregated form which is ineffective for surface enhancement but becomes effective for surface enhancement if the target nucleic acid is present in the sample.

The Examiner's reliance on the Abstract of U.S. Patent 6,127,120 is plainly misplaced, as the Abstract fails to provide any teaching or suggestion of the template-specific aggregation of metal surfaces as claimed in claim 1 of the instant application. Indeed, the Abstract is devoid of any discussion on specific aggregation and merely mentions a SER(R)S-active surface. Notably, a SER(R)S-active surface is defined at column 11, lines 5 through 8, as "any suitable surface, usually metallic, which gives rise to enhancement of the Raman effect." The enhancement is preferably by an aggregation of metal colloid particles (column 11, lines 9-14). Moreover, the metal colloid particles are described as carefully being prepared as unaggregated colloids that are to be "aggregated immediately prior to use" (column 11, lines 20-29). U.S. Patent 6,127,120 also teaches that the aggregated colloids are "ideally formed in situ in the detection sample" because of potential stability issues (column 11, lines 37-41). Applicants submit, however, that U.S. Patent 6,127,120 only teaches employing polyamines such as spermine to control the aggregation process (column 11, lines 42-46). Clearly, the use of spermine and other polyamines to control the aggregation process is not the same as employing metal surfaces which are ineffective for aggregation unless presented with a target nucleic acid, as claimed in the instant application. Therefore, the Abstract fails to teach each and every aspect of the claimed invention.

The Examiner also cites claims 1, 2, 8, and 36 in support of the §102(e) rejection. Here again the cited claims fail to teach metal colloids that aggregate only in the presence of target nucleic acid. Claims 1 and 2 of U.S. Patent 6,127,120 merely speak of the SER(R)S-active surface

Inasmuch as U.S. patent 6,127,120 does not identically disclose the claimed invention, the rejection of claims 1, 5, 6, 8-13, 15-19, and 37 under 35 U.S.C. §102(e) is untenable and should, therefore, be withdrawn.

CLAIMS 7 AND 14 ARE NOT OBVIOUS OVER U.S. PATENT 6,127,120

The Examiner has rejected claims 7 and 14 under 35 U.S.C. §103(a) as allegedly obvious over the disclosure in U.S. Patent 6,127,120. The Examiner asserts that while the inventions claimed in claims 7 and 14 are not specifically taught by U.S. Patent 6,127,120, the claimed subject matter allegedly involves just mere "routine optimization parameters" and therefore is *prima facie* obvious from U.S. Patent 6,127,120.

As set forth in the January 27, 2003 response to the August 27, 2002 Official Action, claims 7 and 14, as dependent claims, must be held patentable over U.S. Patent 6,127,120 because the claims from which they depend are patentable over U.S. Patent 6,127,120. In re Fine, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988).

Moreover, in order to establish a *prima facie* case of obviousness, "all the claim limitations must be taught or suggested by the prior art." MPEP §2143.01; In re Royka, 180 U.S.P.Q 580 (CCPA 1974). As argued hereinabove, U.S. Patent 6,127,120 fails to teach or suggest "aggregation of said metal ... dependent on the presence of said target nucleic acid" as required in claim 1.

Accordingly, the 35 U.S.C. §103 rejection of claims 7 and 14 based on U.S. Patent 6,127,120 is improper and should be withdrawn.

CONCLUSION

In view of the foregoing remarks, it is respectfully urged that the rejections set forth in the August 4, 2003 Official Action be withdrawn and that this application be

and are silent with regard to aggregation caused only by the presence of the specific target nucleic acid. Claims 8 and 36 of U.S. Patent 6,127,120, which are dependent on claims 1 and 2, respectively, state that the SER(R)S-active surface "comprises an aggregation of silver colloid particles," but fail to describe the conditions under which the silver colloid particles aggregate. Thus, claims 8 and 36 do not provide the requisite teaching that aggregation be caused by and occur in the presence of the target nucleic acid.

Additionally, the Examiner cites column 13, lines 37-43 and 57-65 and column 38, lines 22-25 in support of the §102(e) rejection. At column 13, lines 37-43 and 57-65, U.S. Patent 6,127,120 teaches using spermine to promote aggregation of the colloid. Similarly, column 38, lines 22-25 refers to the addition of spermine hydrochloride to promote "formation of stable colloidal aggregates." As stated hereinabove, the instant invention does not depend on polyamines to effect the aggregation of the metal surfaces, but rather the aggregation of the metal surfaces of the instant invention is effected by the presence of the target nucleic acid.

The Examiner also cites Examples 1-9 in support of the §102(e) rejection. Applicants have closely reviewed the cited Examples and have identified only two references to aggregation not already discussed hereinabove. Specifically, at column 39, lines 19 through 21, U.S. Patent 6,127,120 refers to the formation of aggregated colloids, but fails to disclose the conditions under which the aggregates are formed. The cited passage merely describes how the dye may be conformationally altered due to the aggregate colloid. Additionally, at column 39, lines 27 through 31, the superiority of employing spermine in comparison to poly(L-lysine) in controlling the size of the aggregated colloid is discussed. Applicants again submit that U.S. Patent 6,127,120 is silent with respect to aggregation of colloid that is target nucleic acid dependent.

passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

Respectfully submitted,

DANN, DORFMAN, HERRELL AND SKILLMAN
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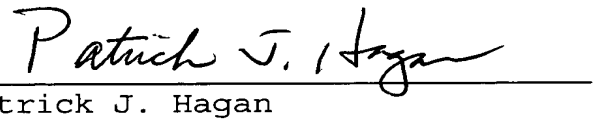
By 

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